Emergency Contraception:
A Cost-Effective Approach to Preventing Unintended Pregnancy†

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This presentation is intended to provide each participant with an understanding of:

- Efficacy, safety, and barriers to use of emergency contraceptives in the United States
- Strategies for promoting awareness and use of emergency contraception
- Cost-effectiveness of emergency contraception
- Important clinical take-home messages about emergency contraceptive pills

Half of all pregnancies in the United States are unintended: there were 3.0 million in 1994 alone, the last year for which data are available.[1] Emergency contraception, which prevents pregnancy after unprotected sexual intercourse, has the potential to reduce significantly the incidence of unintended pregnancy and the consequent need for abortion.[2] Emergency contraception is especially important for outreach to the 3.1 million women at risk of pregnancy but not using a regular method[3] by providing a bridge to use of an ongoing contraceptive method. Although emergency contraceptives do not protect against sexually transmitted infection, they do offer reassurance to the 7.9 million women who rely on condoms for protection against pregnancy[3] in case of condom slippage or breakage. Emergency contraceptives available in the United States include emergency contraceptive pills (ECPs), minipills, and the copper-T intrauterine device (IUD).[4,5,6]

Emergency Contraceptive Pills (ECPs)

ECPs are ordinary birth control pills containing the hormones estrogen and progestin. Although this therapy is commonly known as the morning-after pill, the term is misleading; ECPs may be initiated sooner than the morning after—immediately after unprotected intercourse—or later—for at least 72 hours after unprotected intercourse. The only hormones that have been studied in clinical trials of ECPs are the estrogen ethinyl estradiol and the progestin levonorgestrel or norgestrel (which contains two isomers, only one of which—levonorgestrel—is bioactive). These are found in ten brands of combined oral contraceptives available in the United States as well as one dedicated ECP product (Table 1).[7]

Effectiveness. Use of ECPs reduces the risk of pregnancy by about 75%.[8,9] This statement does not mean that 25% of women using ECPs will become pregnant. Rather, if 100 women have unprotected intercourse once during the second or third week of their cycle, about 8 would become pregnant; following treatment with ECPs, only 2 would become pregnant: a 75% reduction. The current treatment schedule is one dose within 72 hours after unprotected intercourse, and a second dose 12 hours after the first dose. Research suggests that ECPs are not more effective when started

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earlier or less effective when started later in the 72-hour window,[10] and it is biologically implausible that efficacy would abruptly plummet to zero after 72 hours.[11] This finding has two clinical implications. First, clinical protocols that deny treatment beyond 72 hours seem excessively restrictive, particularly if the alternative of emergency insertion of a copper-T IUD is not immediately available or appropriate. Second, a recommendation to take the first dose as soon as possible might well be counterproductive in circumstances when taking the second dose 12 hours later would be difficult; for example, a woman who took her first dose at 3 p.m. immediately following discovery of a burst condom might understandably fail to take the second dose at 3 a.m. The goal should be to make the therapy as user-friendly as possible.[12] However, a recent large study by the World Health Organization found that effectiveness declined significantly with increasing delay between unprotected intercourse and the initiation of treatment.[13] Given the conflicting evidence, this important issue remains unresolved.

Side Effects. About 50% of women who take ECPs experience nausea and 20% vomit.[8] If vomiting occurs within 2 hours after taking a dose, some clinicians recommend repeating that dose. The results of one study suggest that ECPs containing levonorgestrel have an incidence of side effects substantially lower than do ECPs containing norgestrel;[14] see note *c* to Table 1 for information on progestins in ECPs. Non-prescription anti-nausea medicines such as meclizine may reduce the risk of nausea when taken 0.5 to 1.0 hour before ECPs (see Appendix for dosage). Anti-nausea medicines are not routinely offered in the United States. Instead, many providers of ECPs recommend that women take them with food to reduce the risk of nausea, although no data other than anecdotes exist to validate this advice.

Safety. Almost all women can safely use ECPs. The only absolute contraindication to use of ECPs is confirmed pregnancy, simply because ECPs will not work if a woman is pregnant. Treatment may not be appropriate for those who have an active migraine with marked neurological symptoms or crescendo migraine.[15] Given the very short duration of exposure and low total hormone content, ECP treatment can be considered safe for women who would ordinarily be cautioned against use of combined oral contraceptives for ongoing contraception. Although no changes in clotting factors have been detected following ECP treatment,[16] progestin-only pills or insertion of a copper IUD may be preferable to use of ECPs for a women who has a history of stroke or blood clots in the lungs or legs and wants emergency contraceptive treatment. All three of these conditions (pregnancy, migraine, or history of thromboembolism) are identified through medical history screening, so most women requesting ECPs can be evaluated via telephone, without need for an office visit, pelvic exam or laboratory tests.

There have been no conclusive studies of births to women who were already pregnant when they took ECPs or following failure of ECPs. However, there are two observations that provide reassurance for any concern about birth defects.[5] First, in the event of treatment failure, ECPs are taken long before organogenesis starts so that they should not have a teratogenic effect. Second, studies that have examined births to women who inadvertently continued to take oral contraceptives without knowing they were pregnant have found no increased risk of birth defects.[17,18,19] The FDA removed warnings about adverse effects of oral contraceptives on the fetus from the package insert several years ago.[20]

Mechanism of Action. Several clinical studies have shown that ECPs can inhibit or delay ovulation.[21,22,23] This is an important mechanism of action and may explain ECP effectiveness when used during the first half of the menstrual cycle, before ovulation has occurred. Some studies have shown histologic or biochemical alterations in the endometrium after treatment with

Barriers to Use of Emergency Contraception

The lack of a product specifically packaged, labeled, and marketed as an emergency contraceptive was a major obstacle to more widespread use of emergency contraception in the United States until recently (the fall of 1998). Although the Food and Drug Administration (FDA) has not specifically approved regular combined or progestin-only birth control pills or IUDs for emergency contraception, providing these products for this indication is legal. Once a medication or device has been tested and approved for one use, it is a legal and medically accepted practice to prescribe it for other appropriate uses.[33] For example, many women take birth control pills not to prevent pregnancy, but to regulate their menstrual periods, to decrease menstrual cramping, or to prevent the recurrence of ovarian cysts. The FDA's reproductive health drugs advisory committee reviewed research concerning ECP treatment in 1996 and concluded that existing data were sufficient to document the safety and efficacy of this regimen, and the agency then took the unusual action of publishing in the *Federal Register* a notice declaring ECPs to be safe and effective:

> The Food and Drug Administration (FDA) is announcing that the Commissioner of Food and Drugs (the Commissioner) has concluded that certain combined oral contraceptives containing ethinyl estradiol and norgestrel or levonorgestrel are safe and effective for use as postcoital emergency contraception.... The Commissioner bases this conclusion on FDA's review of the published literature concerning this use, FDA's knowledge of the safety of combined oral contraceptives as currently labeled, and on the unanimous conclusion that these regimens are safe and effective made by the agency's Advisory Committee for Reproductive Health Drugs at its June 18, 1996 meeting.[20: 8610,8611]

Even though some doctors have been prescribing emergency contraceptives since the 1970s, no company marketing oral contraceptives or IUDs for ongoing contraception has applied to the FDA to market these products for emergency use. While considerable international research attests to the safety and efficacy of emergency contraceptives, manufacturers cannot market or advertise these products for postcoital use until they seek and gain formal FDA approval for this specific purpose. Without commercial promotion, it is not surprising that physicians prescribe emergency contraceptives infrequently and rarely provide information about emergency contraception to women during routine visits. As a consequence, very few women know that emergency contraception is available, effective, and safe.[34] A recent college campus survey found that while nearly all students were aware of ECPs and knew they were available at the college health center—because of an effective publicity campaign—few knew that ECPs were ordinary combined oral contraceptives, and many could not distinguish ECPs from mifepristone, a medication taken to induce abortion after pregnancy has been confirmed.[35]

One objection to making ECPs more widely available is the concern that women who know they can use ECPs may become less diligent with their ongoing contraceptive method. There are several considerations that lessen this concern. If used as an ongoing method, ECP therapy would be far less effective than any other contraceptive method; therefore, continued use would not be a rational choice. Moreover, one in two women experiences nausea and one in five women vomits after taking ECPs. If anti-nausea medicines are used, the incidence of nausea and vomiting might be halved, but not eliminated. This risk is likely to dissuade such users from having unprotected intercourse often. Reported evidence suggests that making ECPs more widely available does not

increase risk-taking and may reduce the incidence of unintended pregnancy[36] and that women who are the most diligent about ongoing contraceptive use are those most likely to seek emergency treatment.[37] And finally, even if ECP availability did adversely affect regular contraceptive use, women are entitled to know about all contraceptive options.

To help educate women and men about emergency contraception, the Reproductive Health Technologies Project in Washington and the Office of Population Research at Princeton University sponsor the toll-free Emergency Contraception Hotline (1-888-NOT-2-LATE) and the Emergency Contraception Website (http://opr.princeton.edu/ec/). Since it was launched on February 14, 1996, the Hotline has received more than 100,000 calls. More detailed information is available on the Emergency Contraception Website, which has received more than 250,000 hits since it was launched in October 1994. Both the Hotline and Website are completely confidential, available 24 hours a day in English and Spanish, and offer names and telephone numbers of providers of emergency contraception located near the caller's area. The Reproductive Health Technologies Project has received funding from several foundations to work with the advertising and public relations firm Elgin DDB to develop public service announcements for print, radio, television, and outdoor venues. During the last year, a public education campaign was launched in five test cities (Chicago, Los Angeles, Miami, San Diego, and Seattle) in partnership with a coalition of local organizations and clinicians in each area. A paid advertising campaign was launched in Philadelphia and Seattle in July 1998.

Cost-Effectiveness

Use of ECPs or emergency minipills reduces expenditure on medical care by preventing unintended pregnancies, which are very costly. Insertion of a copper-T IUD is not cost saving in the United States when used solely as an emergency contraceptive. Unlike the other two alternatives, however, insertion of a copper-T IUD can provide continuous contraceptive protection for up to 10 years thereafter, producing savings if used as an ongoing method of contraception for as little as four months.[38] ECPs are cost-effective regardless of whether they are provided when the emergency arises or provided beforehand as a routine preventive measure.[7,39]

Not only would making emergency contraception more widely available save medical care dollars, but also additional social cost savings would result. These include not only the monetary costs of unwanted pregnancies and births but also the considerable psychological costs of unintended pregnancy. Moreover, the average medical care cost of unintended births is likely to be greater than the average cost of all births.[40]

Emergency contraceptives would be even more cost-effective in the United States if they were not inefficiently packaged. In other countries, specifically packaged and labeled products are available. In the United Kingdom, for instance, a packet of four PC4 tablets—enough for one course of therapy—is sold by Schering to the National Health Service for $2.20.[41] Similarly, in many countries, a tablet containing the 0.75 mg levonorgestrel found in 20 Ovrette minipills is available. In Malaysia, a brand called Postinor (marketed as a routine postcoital contraceptive, not as an emergency contraceptive) costs about $3-6 for a ten-pill strip.[41] Postinor-2 (a two-pill strip of Postinor tablets specifically packaged and labeled as an emergency contraceptive) will be marketed

in many countries by the Hungarian pharmaceutical company Gedeon Richter. Because of the lower incidence of side effects and greater efficacy, the levonorgestrel-only regimen will replace emergency contraceptive pills containing both estrogen and progestin. Although such products would undoubtedly cost more in the United States than in many other countries, specifically labeled emergency contraceptives would be more convenient for women and providers.

Conclusion

One of every two women aged 15-44 in the United States has experienced at least one unintended pregnancy.[1] Unintended pregnancy is a major public health problem that affects not only the individuals directly involved but also society.[40] Insurers in both the public and private sectors generally cover the medical costs of unintended pregnancy outcomes, with coverage for abortion showing the most variation. Some private insurers provide broad coverage for all contraceptive methods, but most do not.[42] Public payers generally provide broader contraceptive coverage than private payers, although payment levels often are low, perhaps low enough to limit access.[43] Extending explicit coverage to emergency contraception would result in cost savings by reducing the incidence of unintended pregnancy. Making emergency contraceptives more widely available in the United States is one of the most important steps that can be taken to reduce the incidence of unintended pregnancy and the consequent need for abortion.[2,7,44]

Several service delivery innovations would also enhance the potential for emergency contraception to reduce significantly the number of unintended pregnancies. Perhaps the greatest impact would result from changing provider practices so that women seen by primary and reproductive health care clinicians would be routinely informed about emergency contraception before the need arises. The recent clinical practice pattern issued by the American College of Obstetricians and Gynecologists[45] should help clinicians achieve this goal. Additional resources include a monograph of legal issues for health care providers of ECPs produced by the Center for Reproductive Law and Policy[46] and a provider packet developed by the Program for Appropriate Technology in Health[47] and endorsed by many medical organizations (including the American Medical Association, the American College of Obstetricians and Gynecologists and Planned Parenthood Federation of America). Information could be provided to women (and men!) during counseling or by posters, brochures, audio or video cassettes, or wallet cards. Access would be enhanced if clinicians advertised emergency contraception services and if emergency contraceptives were prescribed by telephone without the need for an office visit. A more proactive step would be to prescribe or dispense emergency contraceptive pills to women in advance so the therapy would be immediately accessible if the need arises. Availability would also be enhanced if companies sought FDA approval for and then actively promoted emergency contraceptives. The 1996 FDA notice[20] in the *Federal Register* declaring ECPs to be safe and effective made gaining approval far easier in addition to giving explicit official sanction for ECP use, and the health care company Gynétics gained FDA approval for Preven, a specifically labeled and dedicated ECP, in September 1998.

Table 1. Twelve products that can be used for emergency contraception in the United States[a]

Brand	Manufacturer	Pills per Dose[b]	Ethinyl Estradiol per Dose (µg)	Levonorgestrel per Dose (mg)[c]
Preven	Gynétics	2 blue pills	100	0.50
Ovral	Wyeth-Ayerst	2 white pills	100	0.50
Alesse	Wyeth-Ayerst	5 pink pills	100	0.50
Levlite	Berlex	5 pink pills	100	0.50
Nordette	Wyeth-Ayerst	4 light-orange pills	120	0.60
Levlen	Berlex	4 light-orange pills	120	0.60
Levora	Watson	4 white pills	120	0.60
Lo/Ovral	Wyeth-Ayerst	4 white pills	120	0.60
Triphasil	Wyeth-Ayerst	4 yellow pills	120	0.50
Tri-Levlen	Berlex	4 yellow pills	120	0.50
Trivora	Watson	4 pink pills	120	0.50
Ovrette	Wyeth-Ayerst	20 yellow pills	0	0.75

Notes:

[a] Preven is the only dedicated product specifically marketed for emergency contraception. Ovral, Alesse, Levlite, Nordette, Levlen, Levora, Lo/Ovral, Triphasil, Tri-Levlen, and Trivora have been declared safe and effective for use as ECPs by the U.S. Food and Drug Administration.[20] Outside the United States, emergency contraceptive products are specifically packaged, labeled, and marketed. These have more convenient dosing schedules than all but one of the regimens listed above. The German pharmaceutical company Schering markets a four-pill strip with each pill—identical to Ovral—containing 50 µg ethinyl estradiol and 0.50 mg norgestrel under the brand name PC4 in the United Kingdom; PC4 was pulled from the market in New Zealand after regulatory authorities there switched its status from prescription to over-the-counter. Schering also markets a four-pill strip with each pill containing 50 µg ethinyl estradiol and 0.25 mg levonorgestrel under three brand names: E-Gen-C in South Africa, NeoPrimovlar in Finland, and Tetragynon in Denmark, Germany, Norway, Switzerland and Sweden. The Hungarian pharmaceutical company Gedeon Richter plans to market the levonorgestrel-only product Postinor-2, a two-pill strip with each pill containing 0.75 mg levonorgestrel, with each pill equivalent to 20 Ovrette tablets.

[b] The treatment schedule is one dose within 72 hours after unprotected intercourse, and another dose 12 hours later.

[c] The progestin in Ovral, Lo/Ovral, and Ovrette is norgestrel, which contains two isomers, only one of which (levonorgestrel) is bioactive; the amount of norgestrel in each tablet is twice the amount of levonorgestrel.